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Sentinel lymph node mapping for 385 gastric cancer patients

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ABSTRACT

Background: The objectives were to investigate the accuracy of sentinel lymph node (SLN) biopsy, detect the predictors for undetected or false-negative cases, evaluate the indications for SLN-navigated gastrectomy, and characterize the problems of SLN mapping in gastric cancer. The SLN concept may be applicable to early gastric cancer, particularly clinical T1N0M0 or T2N0M0 with tumor diameter ≤4 cm.

Methods: A total of 385 consecutive patients diagnosed with cT1N0M0 or cT2aN0M0 operable gastric cancer from April 1999 to December 2007 underwent radical gastrectomy with SLN mapping. SLNs were identified using radio-guided and dye-guided methods. Predictors for undetected or false-negative cases on SLN mapping were examined by multivariate regression analysis.

Results: The detection rate of hot and/or blue nodes was 96.6% (372 of 385). The accuracy of metastatic status based on SLNs was 98.9% (368 of 372) for all cases in whom SLNs could be detected. Furthermore, the accuracy of metastatic status based on SLNs was 99.1% (344 of 347) in cT1 gastric cancer and 96.0% (24 of 25) in cT2 gastric cancer. Pathologically, the tumors invaded to the muscularis propria or deeper in three of four false-negative cases. All but one case had metastatic lymph nodes within the sentinel basins. In terms of 5-y recurrence free survival, positive SLN cases (SLN(+)) had a worse prognosis than negative SLN cases (SLN(−); $P = 0.008$). Moreover, SLN(+) and non-SLN(−) cases (SLN(+)/non-SLN(−)) had a similar prognosis as SLN(+) and non-SLN(+) cases (SLN(+)/non-SLN(+)) ($P = 0.511$). On multivariate regression analysis, undetected or false-negative cases were significantly associated with the time period.

Conclusions: The present results appeared to validate the SLN concept for untreated cT1 gastric cancer with tumor diameter ≤4 cm. SLN mapping may provide an effective method of staging the lymph node status of patients undergoing minimized gastrectomy. Sentinel basin dissection guards against the possibility of leaving positive lymph nodes. Stabilization of the procedure and experience with SLN mapping in gastric cancer might decrease undetected or false-negative cases.

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1. Introduction

In the past decades, radical resection with lymphadenectomy for gastric cancer improved locoregional disease control and also improved survival in Far East [1]. The necessary extent of lymph node dissection has been heavily debated and controversial. Recently in Western countries also, D2 lymphadenectomy is recommended as the appropriate surgical approach for patients with resectable gastric cancer because of its long-term survival benefit. However, the routine D2 procedure has also been associated with significantly higher postoperative mortality, morbidity, and reoperation rates [2].

Meanwhile, the popularization of medical examinations and improvements in diagnostic technology make it possible to detect gastric cancer at earlier stages. Many of these patients have been cured by surgical treatment. Recently, laparoscopic-assisted gastrectomy has been improved and standardized. Therefore, the short-term quality of life of these patients is now considered to be better than before. However, such patients have suffered from the sequelae of gastrectomy, such as dumping syndrome, postvagotomy symptoms, and so on, over extended periods, even though some cases had no pathological lymph node metastases. The rate of lymph node metastasis reaches 10% in pathological mucosal gastric carcinoma, 25% in submucosal tumor, 45% in muscularis propria tumor, and 70% in subserosa tumor [3,4]. In fact, many resectable early-stage gastric cancers have no lymph node metastases. Accurate assessment of node status is mandatory to avoid unnecessary extended lymphadenectomy in node-negative patients who may not get the full benefit of the standard D2 dissection.

Given these problems, an individualized surgical procedure is needed, taking into account both curability and after effects, instead of a uniform method. The sentinel lymph node (SLN) concept may make it possible to select the appropriate extent of lymph node dissection to avoid unnecessary lymphadenectomy in node-negative patients.

The SLN first receives lymphatic drainage from the tumor site [5]. The SLN concept that the SLNs are the possible site of first metastasis via the lymphatic route and that the pathological status of the SLN can predict metastases to all other downstream lymph nodes, has been evaluated in various solid tumors. We previously developed SLN mapping in gastric cancer and reported the procedure for the first time [6–9]. Some investigators demonstrated that the SLN concept can be applied in patients with early gastric cancer, in particular clinical T1N0M0 or T2N0M0 with a tumor diameter of $\leq$4 cm [10–12].

The present study is the largest single institutional report of SLN mapping in gastric cancer, to the best of our knowledge. The primary aim of the present work was to investigate the accuracy of the SLN of gastric cancer in our institution and detect the predictors for undetected or false-negative cases, focusing on the indication for SLN-navigated gastrectomy. These results supported the fundamental direction of sentinel node navigation surgery in gastric cancer, which involves functional preservation and is a minimally invasive surgical technique.

2. Materials and methods

2.1. Patients

All patients diagnosed with cT1N0M0 or cT2N0M0 operable primary gastric cancer at Keio University Hospital (Tokyo, Japan) during the period from April 1999 to December 2007 were enrolled in this study. Criteria for eligibility were, in principle, clinical T1N0M0 or T2aN0M0 gastric cancer according to the Union for International Cancer Control (sixth edition, 2002). The patients who obviously had surgical T3 tumor and those for whom endoscopic treatment was indicated were excluded from this analysis. The part of this cohort has been previously reported [13].

All 385 patients underwent a radical gastrectomy and lymphadenectomy with SLN mapping with their informed consent. (Table 1) The average age of the patients was 60.0 y (range, 26–86 y).

Pathologic tumor size was $<$4.0 cm in 286 (74.3%) patients and $\geq$4.0 cm in 99 (25.7%) patients. Sixty-one (15.8%) tumors were in the upper third of the stomach, 224 (58.2%) in the middle third, and 100 (26.0%) in the lower third. Thirty-four (8.8%) patients underwent total gastrectomy, 256 (66.5%) distal gastrectomy, 44 (11.4%) proximal gastrectomy, and 51 (13.2%) underwent transected gastrectomy or pylorus-preserving gastrectomy.

2.2. SLN mapping procedures

A double tracer method with radioactive tracer and blue dye (1% isosulfan blue (Lymphazurin; U.S. Surgical (a division of Tyco Healthcare Group LP), Norwalk, CT or indocyanine green; Daiichi Sankyo, Tokyo, Japan)) was used, as previously described [9–11]. The day before surgery, a 2.0-mL volume of technetium-99m tin colloid solution (150 Bq) was injected at four points around the primary lesion into the submucosal layer endoscopically. At the beginning of surgery, the blue dye was injected in a similar way. Intraoperative radio-labeled SLN sampling was performed using a handheld gamma probe (GPS Navigator; Sheen Man Co, Ltd., Osaka, Japan). Radio-labeled SLNs were defined as hot nodes containing ten times more radioactivity than surrounding tissue. Blue-dyed SLN (blue node) sampling was based on visual evaluation; blue nodes were identified through the afferent lymphatic flow. Finally, the hot and/or blue nodes were defined as the SLNs. Not all SLNs were picked up. SLN biopsy was followed by conventional D1 to D2 gastrectomy based on the Japanese guideline [14]. A skilful surgical team has sequentially performed all gastrectomy and SLN mapping.

2.3. Lymph node specimens

SLNs and the other lymph nodes were examined separately. In virtually all cases, the SLN was immediately bisected during surgery, and frozen sections were examined histologically. The remaining SLN was then processed routinely for H&E staining. All lymph nodes including SLNs were examined in multiple permanent sections.